INTERNATIONAL PRELIMINARY Inte

Re Item I Basis of the opinion

1. Application as filed.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1. Reference is made to the following documents:
 - D1: SAGATOVA F ET AL.: 'Enzymatic conversion of phosphatidylcholine to phosphatidylglcerol' APPLIED BIOCHEMISTRY AND MICROBIOLOGY, vol. 32, no. 5, 1996, pages 452-456, XP000957684 NEW YORK, NY, US ISSN: 0003-6838
 - D2: ANTHONSEN T ET AL: 'Phospholipids hydrolysis in organic solvents catalysed by immobilised phospholipase C' JOURNAL OF MOLECULAR CATALYSIS B-ENZYMATIC, (4 JAN 1999) VOL. 6, NO. 1-2, PP. 125-132. PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS., XP000957601
 - D3: DATABASE WPI Week 8813 Derwent Publications Ltd., London, GB; AN 1988-087107 XP002151651 'Phospholipid prodn. by reacting a phospholipid material and a reactor substance by contacting with phospholipase D' & JP 63 036791 A (NIPPON OILS & FATS CO LTD), 17 February 1988 (1988-02-17)
- 2. The subject-matter of <u>claims 1-14</u> appears to fulfill the requirements of Article 33 (2) and (3) PCT.
- 2.1 Although D1, which is considered to represent the closest prior art, discloses a method of conducting an enzyme-catalysed hydrolysis of phosphatidylcholine in a lecithin-silica gel-water system (D1 page 452, column 1, materials and methods), , wherein the enzyme used is Phospholipase D at concentrations higher than 3 mg/ml (D1, page 454, Figure 3), said document does not teach or suggest the possibility that a liposomal environment would have been beneficiary for high

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scale and high conversion rate (comparing the present application and D1) from phosphatidylcholine (PC) to phosphatidyl glycerol. Furthermore, D1 discloses different ratios between PC and silica gel than the ones disclosed in the present application and, according to figure 5 of D1 a higher ratio (such as in the present application) would result in the decrease in the yield of conversion.

2.2 Both D2 and D3 disclose a method of conducting an enzyme-catalysed hydrolysis of phosphatidylcholine using silica gel (D2, page 125, abstract, D3 whole document), wherein the silica gel used is silica gel 60 from Merck, which includes mean particles of 15 μm, in D2 (D2, page 127, column 1, lines 17 and 18) and a silica gel with preferable size for mean particles between 0.02 and 0.5 mm in D3 (D3 whole document).

The enzyme used is Phospholipase C in D2 and Phospholipase D in D2 (D2, page 125, abstract, D3 whole document).

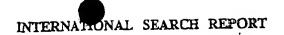
However, both documents do nor disclose or suggest a liposomal system for said conversion. Said system would allow the reaction to be performed in an aqueous environment (in both D2, page 126, column 1, lines 27 and 28, and D3, whole document, water content is reduced as small as possible) which is suitable for pharmaceutical and/or nutritional purposes whereas systems requiring the use of organic solvents for large scale conversion are often not suitable for the above mentioned purposes.

Hence, <u>claims 1-14</u> of the present Application appears to fulfill the requirements of Article 33 (2) and (3) PCT.

Re Item VIII

Certain observations on the international application

1. The term "about" used in <u>claim.5</u> is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).



Interne 11 Application No
PCT/IL 00/00350

A. CLASSI	FIGATION OF SUBJECT MATTER C12N9/16 C12P9/00 C12P		01010/10			
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C. DOCUM	ENTS CONSIDERED TO BE RELEVANT					
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}	European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk					
1	Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax: (+31-70) 340-3016		.Oderwald, H			

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Internal at Application No PCT/IL 00/00350

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C (Continue	ILION) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	,	Relevant to claim No.
AB)	ANTHONSEN T ET AL: "Phospholipids hydrolysis in organic solvents catalysed by immobilised phospholipase C" JOURNAL OF MOLECULAR CATALYSIS B-ENZYMATIC, (4 JAN 1999) VOL. 6, NO. 1-2, PP. 125-132. PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS., XP000957601 the whole document		1-3,6, 11,12
	RAKHIMOV M M ET AL: "PROPERTIES OF PHOSPHO LIPASE D FROM RAPHANUS-SATIVUS" BIOCHEMISTRY (ENGLISH TRANSLATION OF BIOKHIMIYA).		1-6,9-12
	vol. 46, no. 2 PART 1, 1981, pages 197-204, XP000953112 ISSN: 0006-2979 the whole document	,	
	DATABASE WPI Week 8813 Derwent Publications Ltd., London, GB; AN 1988-087107		1-4,6,7
N.	XP002151651 "Phospholipid prodn by reacting a phospholipid material and a reactor substance by contacting with phospholipase n"		
	& JP 63 036791 A (NIPPON OILS & FATS CO LTD), 17 February 1988 (1988-02-17) abstract		
	ALLGYER T T ET AL: "PHOSPHO LIPASE D EC-3.1.4.4 FROM SAVOY CABBAGE PURIFICATION AND PRELIMINARY KINETIC CHARACTERIZATION" BIOCHEMISTRY,		-
16)	vol. 18, no. 24, 1979, pages 5348-5353, XP002151650 ISSN: 0006-2960 cited in the application	•	
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